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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,269	09/16/2002	Olli P. Kallioniemi	4239-62295	8794
36218	7590	10/11/2006	EXAMINER	
KLARQUIST SPARKMAN, LLP 121 S.W. SALMON STREET SUITE #1600 PORTLAND, OR 97204-2988			DEJONG, ERIC S	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TK

Office Action Summary	Application No. 10/088,269	Applicant(s) KALLIONIEMI ET AL.	
	Examiner Eric S. DeJong	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 9-11, 13-40, 64, 65, 67 and 68 is/are pending in the application.
- 4a) Of the above claim(s) 15-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 9-11, 13, 14, 64, 67 and 68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>03/23/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED OFFICE ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/20/2006 has been entered.

Claim Rejections - 35 USC § 112

The rejection of claims 1-5, 9-11, 13, 14, 64, 67, and 68 under 35 USC 112, first paragraph for lack of written description is withdrawn in view of arguments presented by applicants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 9-11, 13, 14, 64, and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the confocal microscope" in lines 4 and 5 of said claim. Claim 64 recites the limitation "the confocal microscope" in lines 4 and 5 of said

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claim. There is insufficient antecedent basis for this limitation in either of claims 1 and 64. Claims 2-5, 9-11, 13, 14, and 67 are also included under this rejection due to their dependence from claim 1.

Claim 5, which depends from claim 3, recites the limitation "the gene of interest" in line 2 of said claim. There is insufficient antecedent basis for this limitation in the claim. For the purpose of continuing examination, claim 5 has been treated as depending from instant claim 4, as claim 4 does provide an antecedent basis for the limitation of "the gene of interest".

Claim Rejections - 35 USC § 102

The rejection of claims 1-5, 10, 11, 13, 14, and 64 under 35 USC 102(e) as being anticipated by Garini et al. is withdrawn in view of amendments made to the instant claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-11, 13, 14, 64, and 67, and 68 are rejected under 35 U.S.C. 103(a) as anticipated by Kahn et al.

The instant claims are drawn to a computer implemented method for counting nucleic acid probe signals in a multi-cell region of interest in a biological spectrum comprising, obtaining a plurality of successive two dimensional image slices of said region taken at different depths along a z-axis via confocal microscopy, distinguishing spatially overlapping nucleic acid probe signals, automatically counting a number of test signals from a test probe, automatically counting a number of reference probe signals, and determining a ratio of the automatically-counted test signals to the automatically counted reference signals.

Kahn et al. sets for the visualization and localization of specific DNA sequences performed by fluorescence in situ hybridization (FISH) using laser scanning confocal microscopy and Factor Analysis of Biomedical Image Sequences (FAMIS) (see Kahn et al., Abstract). The methodology is disclosed as being computer-implemented as image analysis of convention 3D reconstructions of cells were obtained by means of the Image Space software (see Kahn et al., page 277, col. 1, lines 4-14). Kahn et al. sets forth obtaining both sample analysis and construction 3D image of a sample region by collecting a series of 2D of fluorescence images at different sample depths (see Kahn et al. Figures 1A-C, page 227, col. 1, line 5 through page 278, col. 1, line 18 and page 278, col. 1, line 45 through col. 2, line 5). Figure 1C of Kahn et al. sets forth that 2D fluorescence images were obtained at different confocal plants along the z-axis. Kahn et al., and further demonstrates that overlapping fluorescent signals may be distinguished from successive 2D images taken at different sample depths by use of a factor profiles $a(i)$, $b(i)$, and $c(i)$, wherein said factor profiles were derived from 2D images obtained at

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different sample depths. Kahn et al. further sets forth the use of two fluorescent dyes, Fast Red (FR) and Thylozine Orange (TO) as probe labels, wherein said dyes may be used simultaneously (see Kahn et al., page 269, col. 1, line 5 through page 271, col. 2, line 4). FR is disclosed as providing a high quantum yield and was relied upon by Kahn et al. to detect small amounts of DNA sequences in individual cells, which reads on the instantly claimed limitation of a test signal from a test probe. TO was relied upon to counterstain nuclei, which reads on the instantly claimed reference signals from a reference probe. Signals from both FR and TO fluorescently labeled probes are determined from each 2D image sequence and relied upon in the FAMIS application (see Kahn et al., page 273, col. 2, line 11, through page 275, col. 1, line 14).

Kahn et al. further teaches that problems previously resulting from the superposition of fluorescein signals, autofluorescence, and propidium iodide-stained nuclei are resolved when FR and TO spectral features are taken into account by FAMIS (see Kahn et al., page 278, col. 1, lines 20-31 and page 278, col. 2, line 22 through page 279, col. 1, line 18). Kahn et al. sets forth that although TO and FR distributions cannot be distinguished in any single 2D image, FAMIS decomposition of a plurality of 2D image sequences into specific TO and FR distributions permits a multispectral analysis. FAMIS decomposition of a plurality of 2D image sequences results in the generation of factor profiles involves transforming contiguous signals, obtained from successive 2D images, into a single curve that allows for determining which of the successive 2D images contains the strongest probe/reference signal. Direct comparison of decomposed TO and FR distributions obtained from 2D images involves the

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determination of a ratio of TO and FR intensities, which reads on determining a ratio of counted test signals from the test probe and counted reference signals from the reference probe. Further, all comparison of TO and FR fluorescence intensity were performed without reference to either the boundaries of a cell nucleus or of a cell.

Regarding image analysis and the decomposition of images, Kahn et al. sets forth that iterative algorithms are applied by FAMIS in the analysis and computation of combined 2D images into a clustered matrices, which reads on the instantly instant limitations of automatically counting a number of test signals and automatically counting a number of reference signals.

Claim Rejections - 35 USC § 103

The rejection of claims 1-5, 9-11, 13, 14, 64, 67 and 68 under 35 USC 103(a) as being unpatentable over Garini et al. in view of Cabib et al. are withdrawn in view of amendments made to the instant claims.

Response to Arguments

Applicant's arguments with respect to claims 1-5, 9-11, 13, 14, 64, 67, and 68 have been considered but are moot in view of the new grounds of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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John S. Brusca 1 October 2006
JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER